Spontaneous Single-Copy Loss of TP53 in Human Embryonic Stem Cells Markedly Increases Cell Proliferation and Survival.

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Public Summary:
Genomic aberrations have been identified in many human pluripotent stem cell (hPSC) cultures. Commonly observed duplications in portions of chromosomes 12p and 17q have been associated with increases in genetic instability and resistance to apoptosis, respectively. However, the phenotypic consequences related to sporadic mutations have not been evaluated to date. Here, we report on the effects of a single-copy deletion of the chr17p13.1 region, a sporadic mutation that spontaneously arose independently in several subclones of a human embryonic stem cell culture. Compared to cells with two normal copies of chr17p13.1 ("wild-type"), the cells with a single-copy deletion of this region ("mutant") displayed a selective advantage when exposed to stressful conditions, and retained a higher percentage of cells expressing the pluripotency marker POU5F1/OCT4 after 2 weeks of in vitro differentiation. Knockdown of TP53, which is a gene encompassed by the deleted region, in wild-type cells mimicked the chr17p13.1 deletion phenotype. Thus, sporadic mutations in hPSCs can have phenotypic effects that may impact their utility for clinical applications. Stem Cells 2017;35:872-885.

Scientific Abstract:
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